

§Appl. No. 09/965,807  
Amdt. dated December 7, 2004  
Supplemental Reply to Office Action of, July 2, 2004

**Listing of Claims:**

Please **amend** the claims as follows:

<b>Claim 1</b>	<b>(Cancelled)</b>
<b>Claim 2</b>	<b>(Cancelled)</b>
<b>Claim 3</b>	<b>(Cancelled)</b>
<b>Claim 4</b>	<b>(Cancelled)</b>
<b>Claim 5</b>	<b>(Cancelled)</b>
<b>Claim 6</b>	<b>(Cancelled)</b>
<b>Claim 7</b>	<b>(Cancelled)</b>
<b>Claim 8</b>	<b>(Cancelled)</b>
<b>Claim 9</b>	<b>(Cancelled)</b>
<b>Claim 10</b>	<b>(Cancelled)</b>
<b>Claim 11</b>	<b>(Cancelled)</b>
<b>Claim 12</b>	<b>(Cancelled)</b>
<b>Claim 13</b>	<b>(Cancelled)</b>
<b>Claim 14</b>	<b>(Cancelled)</b>
<b>Claim 15</b>	<b>(Cancelled)</b>
<b>Claim 16</b>	<b>(Cancelled)</b>
<b>Claim 17</b>	<b>(Cancelled)</b>
<b>Claim 18</b>	<b>(Cancelled)</b>
<b>Claim 19</b>	<b>(Cancelled)</b>
<b>Claim 20</b>	<b>(Canceled)</b>
<b>Claim 21</b>	<b>(Cancelled)</b>

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**Claim 22 (Previously Presented)** An isolated naturally-occurring mutant human aspartoacylase polypeptide either an altered ability to hydrolyze N-acetyl-aspartic acid to aspartate and acetate, as compared with a wild-type human aspartoacylase, or incapable of hydrolyzing N-acetyl-aspartic acid to aspartate and acetate, and comprising the amino acid sequence SEQ ID NO: 2 of wild-type human aspartoacylase, except for said mutation, which is

E285 > A,

Y231 > X, and/or

A305 > E,

or a naturally-occurring mutant allele of said wild-type human aspartoacylase.

**Claim 23 (Cancelled)**

**Claim 24 (Previously Presented)** A mutant aspartoacylase of claim 22, wherein the glutamic acid at amino acid position 285 is substituted by alanine.

**Claim 25 (Cancelled)**

**Claim 26 (Cancelled)**

**Claim 27 (Cancelled)**

**Claim 28 (Cancelled)**

**Claim 29 (Cancelled)**

**Claim 30 (Cancelled)**

**Claim 31 (Cancelled)**

**Claim 32 (Cancelled)**

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<b>Claim 33</b>	<b>(Cancelled)</b>
<b>Claim 34</b>	<b>(Cancelled)</b>
<b>Claim 35</b>	<b>(Cancelled)</b>
<b>Claim 36</b>	<b>(Cancelled)</b>
<b>Claim 37</b>	<b>(Cancelled)</b>
<b>Claim 38</b>	<b>(Cancelled)</b>
<b>Claim 39</b>	<b>(Cancelled)</b>
<b>Claim 40</b>	<b>(Cancelled)</b>
<b>Claim 41</b>	<b>(Cancelled)</b>
<b>Claim 42</b>	<b>(Cancelled)</b>
<b>Claim 43</b>	<b>(Cancelled)</b>
<b>Claim 44</b>	<b>(Cancelled)</b>
<b>Claim 45</b>	<b>(Cancelled)</b>
<b>Claim 46</b>	<b>(Cancelled)</b>
<b>Claim 47</b>	<b>(Cancelled)</b>
<b>Claim 48</b>	<b>(Cancelled)</b>
<b>Claim 49</b>	<b>(Cancelled)</b>
<b>Claim 50</b>	<b>(Cancelled)</b>
<b>Claim 51</b>	<b>(Cancelled)</b>
<b>Claim 52</b>	<b>(Cancelled)</b>
<b>Claim 53</b>	<b>(Cancelled)</b>
<b>Claim 54</b>	<b>(Cancelled)</b>
<b>Claim 55</b>	<b>(Cancelled)</b>
<b>Claim 56</b>	<b>(Cancelled)</b>
<b>Claim 57</b>	<b>(Cancelled)</b>
<b>Claim 58</b>	<b>(Cancelled)</b>

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**Claim 59** (Cancelled)

**Claim 60** (Cancelled)

**Claim 61** (Cancelled)

**Claim 62** (Cancelled)

**Claim 63** (Previously Presented) A transgenic mouse exhibiting Canavan disease symptoms.

**Claim 64** (Cancelled)

**Claim 65** (Cancelled)

**Claim 66** (Previously Presented) A fragment of a mutant human aspartoacylase of claim 22, comprising an aspartoacylase epitope which is immunologically-effective to elicit antibodies that selectively bind to said human aspartoacylase.

**Claim 67** (Previously Presented) A recombinant wild-type human aspartoacylase capable of hydrolyzing N-acetyl aspartic acid to aspartate and acetate, comprising an amino acid sequence which has a sequence identity of at least 95% to the sequence of SEQ ID NO: 2.

**Claim 68** (Previously Presented) A fragment of a recombinant wild-type human aspartoacylase of claim 67, comprising an aspartoacylase epitope which is immunologically-effective to elicit antibodies that selectively bind to said human aspartoacylase.

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**Claim 69 (Previously Presented)** A pharmaceutical composition, comprising an isolated wild-type human aspartoacylase comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, and a pharmaceutically acceptable carrier.

**Claim 70 (Previously Presented)** An isolated normal human aspartoacylase comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, which is free of other cellular components.

**Claim 71 (Previously Presented)** An isolated normal-type human aspartoacylase comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, which is free of other human proteins.

**Claim 72 (Previously Presented)** A preparation which consists essentially of a wild-type human aspartoacylase comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof.

**Claim 73 (Previously Presented)** An isolated wild-type human aspartoacylase comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, in a concentration which can be administered to a patient at a dosage of 0.1 to 100 U/kg.

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**Claim 74 (Previously Presented)** A wild-type human aspartoacylase comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, produced by

(a) culturing a host cell transformed with a vector comprising a DNA which encodes for a normal human aspartoacylase of claim 80 in a cell culture medium under conditions whereby the aspartoacylase is expressed, and

(b) isolating the thus-produced wild-type aspartoacylase.

**Claim 75 (Previously Presented)** A wild-type human aspartoacylase comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, produced in a bacterium, a fungus, or a non-human mammalian cell.

**Claim 76 (Withdrawn)** An immunologically active anti-aspartoacylase polyclonal or monoclonal antibody specific for an aspartoacylase polypeptide of claim 20.

**Claim 77 (Withdrawn)** An immunologically active anti-aspartoacylase polyclonal or monoclonal antibody specific for an aspartoacylase polypeptide of claim 22.

**Claim 78 (Withdrawn)** A hybridoma producing a monoclonal antibody specific for an aspartoacylase polypeptide of claim 20.

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**Claim 79 (Withdrawn)** A hybridoma producing a monoclonal antibody specific for an aspartoacylase polypeptide of claim 22.

**Claim 80 (Previously Presented)** A recombinant wild-type human aspartoacylase capable of hydrolyzing N-acetyl aspartic acid to aspartate and acetate, comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof.

**Claim 81 (Previously Presented)** A wild-type human aspartoacylase polypeptide purified to homogeneity and capable of hydrolyzing N-acetyl-aspartic acid to aspartate and acetate.

**Claim 82 (Previously Presented)** The aspartoacylase of claim 81 having SEQ ID NO: 2.

**Claim 83 (Previously Presented)** An isolated polypeptide of claim 22 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 84 (Previously Presented)** An isolated polypeptide of claim 66 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

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**Claim 85 (Previously Presented)** An isolated polypeptide of claim 67 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 86 (Previously Presented)** An isolated polypeptide of claim 68 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 87 (Previously Presented)** An isolated polypeptide of claim 71 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 88 (Previously Presented)** An isolated polypeptide of claim 72 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 89 (New)** An isolated wild-type human aspartoacylase capable of hydrolyzing N-acetyl aspartic acid to aspartate and acetate, comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, which is produced by expressing a DNA coding for said aspartoacylase in a host cell.

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**Claim 90** (New) An isolated wild-type human aspartoacylase of claim 89, comprising the amino acid sequence SEQ ID NO: 2.

**Claim 91** (New) An isolated naturally-occurring mutant human aspartoacylase polypeptide having either an altered ability to hydrolyze N-acetyl-aspartic acid to aspartate and acetate, as compared with a wild-type human aspartoacylase, or incapable of hydrolyzing N-acetyl-aspartic acid to aspartate and acetate, and comprising the amino acid sequence SEQ ID NO: 2 of wild-type human aspartoacylase, except for said mutation, which is

E285 > A,

Y231 > X, and/or

A305 > E,

or a naturally-occurring mutant allele of said wild-type human aspartoacylase, wherein said polypeptide is produced by expressing a DNA coding for said aspartoacylase in a host cell.